62081

Patent and Trademark Office

SEARCH REQUEST FORM

Requestor's Name: BERCH

Serial Number: 926477

Date: 3/11/02

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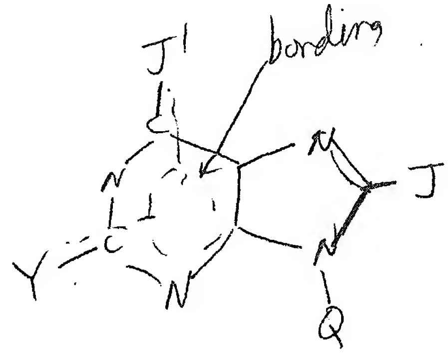
4D15 4E12

Art Unit: 1624

Search Topic:

Please write a detailed statement of search topic. Describe specifically as possible the subject matter to be searched. Define any terms that may have a special meaning. Give examples or relevant citations, authors keywords, etc., if known. For sequences, please attach a copy of the sequence. You may include a copy of the broadest and/or most relevant claim(s).



all J = CH_3, C_2H_5

Q = H or CH_2–⟨ring⟩ O–C-in-a-ring / OJ''

Y = SC / O–(S|P|C=O) / Hal / O–(C(A)(A'))$_{1-5}$–⟨ring⟩

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Date completed: 3/14	**Search Site**	**Vendors**
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CPU time:	**Type of Search**	___ APS
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	___ Bibliographic	___ Other

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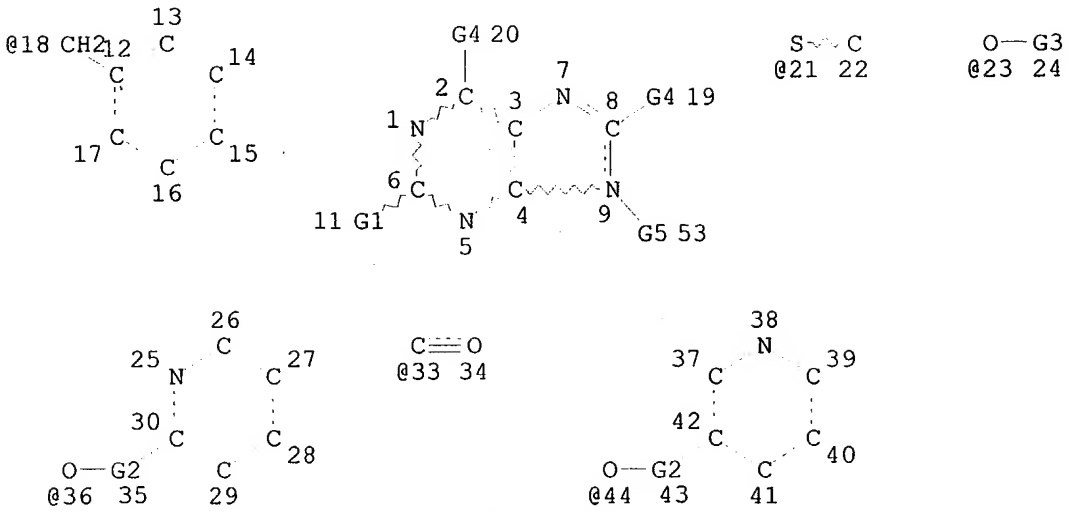

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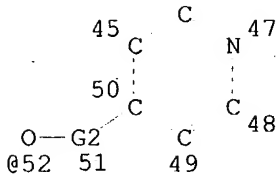
Page 1-A



Page 2-A
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VAR G4=ME/ET
VAR G5=H/18
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NSPEC IS RC AT 22
DEFAULT MLEVEL IS ATOM
DEFAULT ECLEVEL IS LIMITED

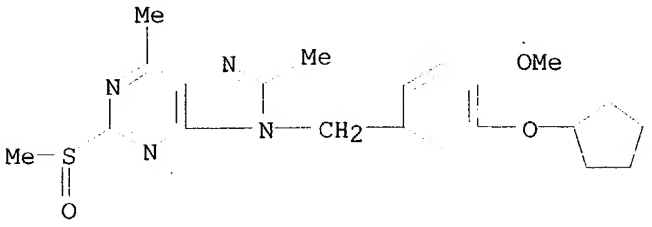
GRAPH ATTRIBUTES:
RING(S) ARE ISOLATED OR EMBEDDED
NUMBER OF NODES IS 50

STEREO ATTRIBUTES: NONE
L5 17 SEA FILE=REGISTRY SSS FUL L4

100.0% PROCESSED 263 ITERATIONS 17 ANSWERS
SEARCH TIME: 00.00.01

Searched by: Mary Hale 308-4258 CM-1 12D16

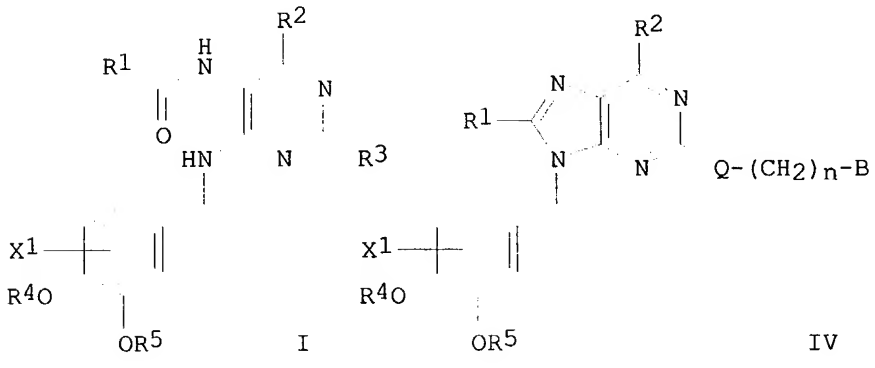
L5 ANSWER 1 OF 17 REGISTRY COPYRIGHT 2002 ACS
RN 331665-29-3 REGISTRY
CN 9H-Purine, 9-[[3-(cyclopentyloxy)-4-methoxyphenyl]methyl]-6,8-dimethyl-2-(methylsulfinyl)- (9CI) (CA INDEX NAME)
OTHER NAMES:
CN 9-(3-Cyclopentyloxy-4-methoxybenzyl)-6,8-dimethyl-2-(methanesulfinyl)purine
FS 3D CONCORD
MF C21 H26 N4 O3 S
SR CA
LC STN Files: CA, CAPLUS

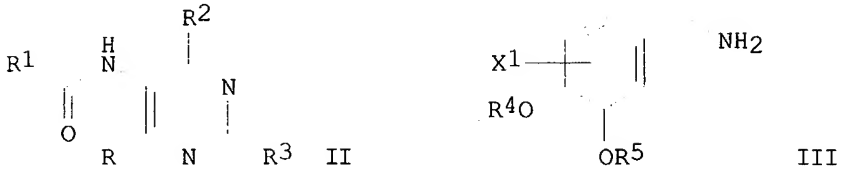


PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

1 REFERENCES IN FILE CA (1967 TO DATE)
1 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 134:252357 Pyrimidine derivatives and method for their preparation. Iwamura, Hiroshi; Tozawa, Takashi; Inokawa, Haruki; Shirasaka, Tadashi (Mitsubishi Chemical Corp., Japan; Mistubishi Tokyo Pharmaceuticals Inc.). Jpn. Kokai Tokkyo Koho JP 2001089458 A2 20010403, 18 pp. (Japanese). CODEN: JKXXAF. APPLICATION: JP 1999-263372 19990917.
GI

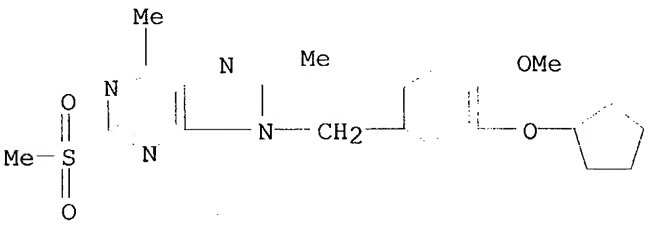




Searched by: Mary Hale 308-4258 CM-1 12D16

AB 5-Acylamino-4-(3,4-dihydroxybenzylamino)pyrimidine derivs. [I; R1, R2 = H, C1-4 alkyl; R3 = (un)substituted C1-10 alkoxy, C6-10 aryloxy, C3-10 cycloalkyloxy, C7-12 aralkyloxy, C1-10 alkylthio, C6-10 arylthio, C3-10 cycloalkylthio, or C7-12 aralkylthio; R4 = C1-4 alkyl, difluoromethyl; R5 = tetrahydropyranyl, C1-7 alkyl, C1-7 haloalkyl, C2-7 alkenyl, bicyclo[2.2.1]hept-2-yl, C3-8 cycloalkyl; X1 = H,halo, NO2] are prepd. by conversion of 4-hydroxy-5-acylaminopyrimidine derivs. (II; R = OH; R1- R3 = same as above) into reactive pyrimidine derivs. II (R = halo, (un)substituted C1-10 alkylsulfonyloxy, C6-10 arylsulfonyloxy, C1-10 dialkyloxyphosphoryloxy, 2,2,2-trifluoroethyloxy; R1-R3 = same as above) and reaction of the latter deriv. with 3,4-dihydroxybenzylamine derivs. (III; R4, R5, X1 = same as above). The above compds. I are useful as intermediates for agrochems. and drugs, in particular 9-(3,4-dihydroxybenzyl)purine antiasthmatics represented by formula [IV; R1, R2, R4 , R5, X1 = same as above; Q = O, S, NHCO, CONH, NH, C1-6 alkyl-NH; n = 0-4; B = (un)substituted Ph, naphthyl, or heterocyclyl; when Q is C1-6 alkyl-NH, n is 1-4 and B is (un)substituted heterocyclyl]. Thus, 4.5 mL Et3N, 12.1 mL POCl3, and 6.50 g 5-acetamido-4-hydroxy-6-methyl-2-methylthiopyrimidine were added to a suspension of 9.62 g benzyltriethylammonium chloride in 65 mL MeCN under ice-cooling and stirred at room temp. for 3 h to give, after workup and silica gel chromatog., 36% 5-acetamido-4-chloro-6-methyl-2-methylthiopyrimidine (V) (2.51 g). Et3N (0.47 mL) was added to a suspension of 350 mg V and 366 mg 3-cyclopentyloxy-4-methoxybenzylamine hydrochloride in 3 mL 2-propanol, heated at 80.degree. with stirring for 3 h, treated with 101 mg 1,4-diazabicyclo[2.2.2]octane, and stirred at 80.degree. for 1.5 to give, after workup and silica gel chromatog., 95% 5-acetamido-4-[(3-cyclopentyloxy-4-methoxybenzyl)amino]-6-methyl-2-methylthiopyrimidine (597 mg). A soln. of the latter compd. (6.04 g) in 50 mL 2-propanol were added 9.3 mL 25% NaOH and 20 mL H2O and stirred at 80.degree. for 3 h to give, after workup, 94% 9-(3-cyclopentyloxy-4-methoxybenzyl)-6,8-dimethyl-2-methylthiopurine.

L5 ANSWER 2 OF 17 REGISTRY COPYRIGHT 2002 ACS
RN 331665-28-2 REGISTRY
CN 9H-Purine, 9-[[3-(cyclopentyloxy)-4-methoxyphenyl]methyl]-6,8-dimethyl-2-(methylsulfonyl)- (9CI) (CA INDEX NAME)
OTHER NAMES:
CN 9-(3-Cyclopentyloxy-4-methoxybenzyl)-6,8-dimethyl-2-(methanesulfonyl)purine
FS 3D CONCORD
MF C21 H26 N4 O4 S
SR CA
LC STN Files: CA, CAPLUS, CASREACT



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

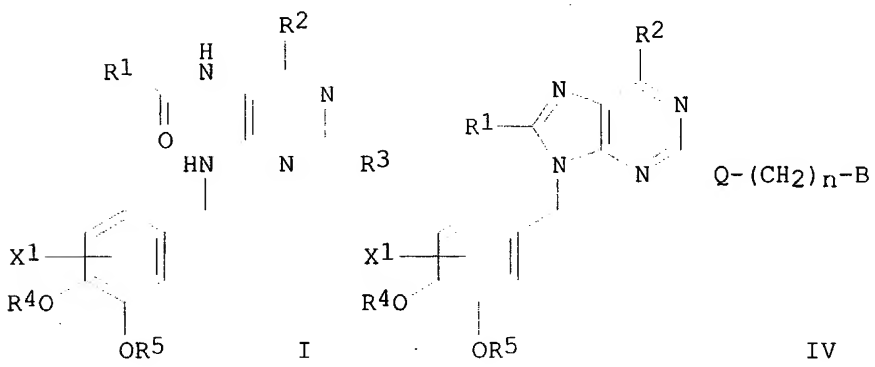
2 REFERENCES IN FILE CA (1967 TO DATE)

Searched by: Mary Hale 308-4258 CM-1 12D16

2 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 134:252357 Pyrimidine derivatives and method for their preparation. Iwamura, Hiroshi; Tozawa, Takashi; Inokawa, Haruki; Shirasaka, Tadashi (Mitsubishi Chemical Corp., Japan; Mistubishi Tokyo Pharmaceuticals Inc.). Jpn. Kokai Tokkyo Koho JP 2001089458 A2 20010403, 18 pp. (Japanese). CODEN: JKXXAF. APPLICATION: JP 1999-263372 19990917.

GI



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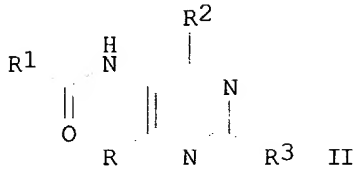

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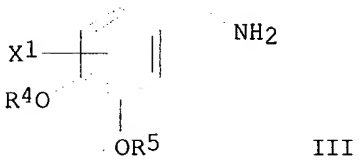

III

AB 5-Acylamino-4-(3,4-dihydroxybenzylamino)pyrimidine derivs. [I; R1, R2 = H, C1-4 alkyl; R3 = (un)substituted C1-10 alkoxy, C6-10 aryloxy, C3-10 cycloalkyloxy, C7-12 aralkyloxy, C1-10 alkylthio, C6-10 arylthio, C3-10 cycloalkylthio, or C7-12 aralkylthio; R4 = C1-4 alkyl, difluoromethyl; R5 = tetrahydropyranyl, C1-7 alkyl, C1-7 haloalkyl, C2-7 alkenyl, bicyclo[2.2.1]hept-2-yl, C3-8 cycloalkyl; X1 = H,halo, NO2] are prepd. by conversion of 4-hydroxy-5-acylaminopyrimidine derivs. (II; R = OH; R1- R3 = same as above) into reactive pyrimidine derivs. II (R = halo, (un)substituted C1-10 alkylsulfonyloxy, C6-10 arylsulfonyloxy, C1-10 dialkyloxyphosphoryloxy, 2,2,2-trifluoroethyloxy; R1-R3 = same as above) and reaction of the latter deriv. with 3,4-dihydroxybenzylamine derivs. (III; R4, R5, X1 = same as above). The above compds. I are useful as intermediates for agrochems. and drugs, in particular 9-(3,4-dihydroxybenzyl)purine antiasthmatics represented by formula [IV; R1, R2, R4 , R5, X1 = same as above; Q = O, S, NHCO, CONH, NH, C1-6 alkyl-NH; n = 0-4; B = (un)substituted Ph, naphthyl, or heterocyclyl; when Q is C1-6 alkyl-NH, n is 1-4 and B is (un)substituted heterocyclyl]. Thus, 4.5 mL Et3N, 12.1 mL POCl3, and 6.50 g 5-acetamido-4-hydroxy-6-methyl-2-methylthiopyrimidine were added to a suspension of 9.62 g benzyltriethylammonium chloride in 65 mL MeCN under ice-cooling and stirred at room temp. for 3 h to give, after workup and silica gel chromatog., 36% 5-acetamido-4-chloro-6-methyl-2-methylthiopyrimidine (V) (2.51 g). Et3N (0.47 mL) was added to a suspension of 350 mg V and 366 mg 3-cyclopentyloxy-4-methoxybenzylamine hydrochloride in 3 mL 2-propanol, heated at 80.degree. with stirring for 3 h, treated with 101 mg 1,4-diazabicyclo[2.2.2]octane, and stirred at 80.degree. for 1.5 to give, after workup and silica gel chromatog., 95% 5-acetamido-4-[(3-cyclopentyloxy-4-methoxybenzyl)amino]-6-methyl-2-methylthiopyrimidine (597

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mg). A soln. of the latter compd. (6.04 g) in 50 mL 2-propanol were added 9.3 mL 25% NaOH and 20 mL H2O and stirred at 80.degree. for 3 h to give, after workup, 94% 9-(3-cyclopentyloxy-4-methoxybenzyl)-6,8-dimethyl-2-methylthiopurine.

REFERENCE 2: 134:252207 Preparation of purine derivatives as intermediate for antiasthmatic agents. Iwamura, Hiroshi; Tozawa, Takashi; Inokawa, Haruki; Shirasaka, Tadashi (Mitsubishi Chemical Corp., Japan; Mistubishi Tokyo Pharmaceuticals Inc.). Jpn. Kokai Tokkyo Koho JP 2001089480 A2 20010403, 13 pp. (Japanese). CODEN: JKXXAF. APPLICATION: JP 1999-263373 19990917.

GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB Purines I [R1, R2 = H, C1-4 alkyl; R3 = OH, alkylsulfonyloxy, arylsulfonyloxy, dialkyloxyphosphoryloxy, CF3CH2O, etc.; R4 = C1-4 alkyl, CHF2; R5 = tetrahydrofuranyl, C1-7 (halo)alkyl, C2-7 alkenyl, etc.; X1 = H, halo, NO2], their salts, hydrates, or solvates are prepd. by cyclization of pyrimidines II [R6, R7, R9, R10, X2 = same as R1, R2, R4, R5, X1 in I; R8 = (un)substituted C1-10 alkyloxy, C6-10 aryloxy, C1-10 alkylthio, C6-10 arylthio, etc.], their salts, hydrates, or solvates. II (R6 = R7 = R9 = Me, R8 = SMe, R10 = cyclopentyl, X2 = H) (prepn. given) was treated with aq. NaOH in 2-propanol at 80.degree. for 3 h to give 94% I (R1 = R2 = R4 = Me, R3 = SMe, R5 = cyclopentyl, X1 = H), which was oxidized and condensed with 4-pyridinepropanol to give I [R1 = R2 = R4 = Me, R3 = 3-(4-pyridyl)propyloxy, R5 = cyclopentyl, X1 = H].

L5 ANSWER 3 OF 17 REGISTRY COPYRIGHT 2002 ACS
RN 331665-27-1 REGISTRY
CN 9H-Purine, 9-[[3-(cyclopentyloxy)-4-methoxyphenyl]methyl]-6,8-dimethyl-2-(methylthio)- (9CI) (CA INDEX NAME)
OTHER NAMES:
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FS 3D CONCORD
DR 331673-10-0
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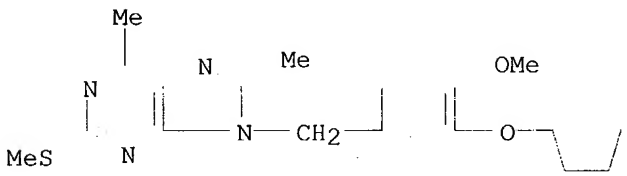
SR CA
LC STN Files: CA, CAPLUS, CASREACT



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

3 REFERENCES IN FILE CA (1967 TO DATE)
2 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 134:252357 Pyrimidine derivatives and method for their preparation. Iwamura, Hiroshi; Tozawa, Takashi; Inokawa, Haruki; Shirasaka, Tadashi (Mitsubishi Chemical Corp., Japan; Mistubishi Tokyo Pharmaceuticals Inc.). Jpn. Kokai Tokkyo Koho JP 2001089458 A2 20010403,

Searched by: Mary Hale 308-4258 CM-1 12D16

18 pp. (Japanese). CODEN: JKXXAF. APPLICATION: JP 1999-263372 19990917.

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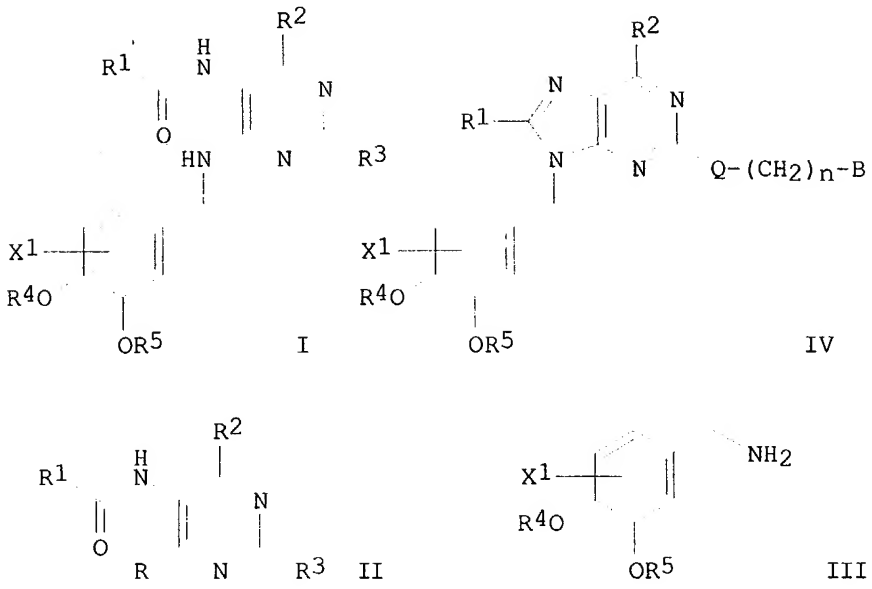


AB 5-Acylamino-4-(3,4-dihydroxybenzylamino)pyrimidine derivs. [I; R1, R2 = H, C1-4 alkyl; R3 = (un)substituted C1-10 alkoxy, C6-10 aryloxy, C3-10 cycloalkyloxy, C7-12 aralkyloxy, C1-10 alkylthio, C6-10 arylthio, C3-10 cycloalkylthio, or C7-12 aralkylthio; R4 = C1-4 alkyl, difluoromethyl; R5 = tetrahydropyranyl, C1-7 alkyl, C1-7 haloalkyl, C2-7 alkenyl, bicyclo[2.2.1]hept-2-yl, C3-8 cycloalkyl; X1 = H,halo, NO2] are prepd. by conversion of 4-hydroxy-5-acylaminopyrimidine derivs. (II; R = OH; R1- R3 = same as above) into reactive pyrimidine derivs. II (R = halo, (un)substituted C1-10 alkylsulfonyloxy, C6-10 arylsulfonyloxy, C1-10 dialkyloxyphosphoryloxy, 2,2,2-trifluoroethyloxy; R1-R3 = same as above) and reaction of the latter deriv. with 3,4-dihydroxybenzylamine derivs. (III; R4, R5, X1 = same as above). The above compds. I are useful as intermediates for agrochems. and drugs, in particular 9-(3,4-dihydroxybenzyl)purine antiasthmatics represented by formula [IV; R1, R2, R4 , R5, X1 = same as above; Q = O, S, NHCO, CONH, NH, C1-6 alkyl-NH; n = 0-4; B = (un)substituted Ph, naphthyl, or heterocyclyl; when Q is C1-6 alkyl-NH, n is 1-4 and B is (un)substituted heterocyclyl]. Thus, 4.5 mL Et3N, 12.1 mL POCl3, and 6.50 g 5-acetamido-4-hydroxy-6-methyl-2-methylthiopyrimidine were added to a suspension of 9.62 g benzyltriethylammonium chloride in 65 mL MeCN under ice-cooling and stirred at room temp. for 3 h to give, after workup and silica gel chromatog., 36% 5-acetamido-4-chloro-6-methyl-2-methylthiopyrimidine (V) (2.51 g). Et3N (0.47 mL) was added to a suspension of 350 mg V and 366 mg 3-cyclopentyloxy-4-methoxybenzylamine hydrochloride in 3 mL 2-propanol, heated at 80.degree. with stirring for 3 h, treated with 101 mg 1,4-diazabicyclo[2.2.2]octane, and stirred at 80.degree. for 1.5 to give, after workup and silica gel chromatog., 95% 5-acetamido-4-[(3-cyclopentyloxy-4-methoxybenzyl)amino]-6-methyl-2-methylthiopyrimidine (597 mg). A soln. of the latter compd. (6.04 g) in 50 mL 2-propanol were added 9.3 mL 25% NaOH and 20 mL H2O and stirred at 80.degree. for 3 h to give, after workup, 94% 9-(3-cyclopentyloxy-4-methoxybenzyl)-6,8-dimethyl-2-methylthiopurine.

REFERENCE 2: 134:252207 Preparation of purine derivatives as intermediate

Searched by: Mary Hale 308-4258 CM-1 12D16

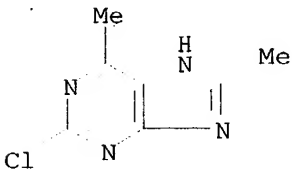
for antiasthmatic agents. Iwamura, Hiroshi; Tozawa, Takashi; Inokawa, Haruki; Shirasaka, Tadashi (Mitsubishi Chemical Corp., Japan; Mistubishi Tokyo Pharmaceuticals Inc.). Jpn. Kokai Tokkyo Koho JP 2001089480 A2 20010403, 13 pp. (Japanese). CODEN: JKXXAF. APPLICATION: JP 1999-263373 19990917.

GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB Purines I [R1, R2 = H, C1-4 alkyl; R3 = OH, alkylsulfonyloxy, arylsulfonyloxy, dialkyloxyphosphoryloxy, CF3CH2O, etc.; R4 = C1-4 alkyl, CHF2; R5 = tetrahydrofuranyl, C1-7 (halo)alkyl, C2-7 alkenyl, etc.; X1 = H, halo, NO2], their salts, hydrates, or solvates are prepd. by cyclization of pyrimidines II [R6, R7, R9, R10, X2 = same as R1, R2, R4, R5, X1 in I; R8 = (un)substituted C1-10 alkyloxy, C6-10 aryloxy, C1-10 alkylthio, C6-10 arylthio, etc.], their salts, hydrates, or solvates. II (R6 = R7 = R9 = Me, R8 = SMe, R10 = cyclopentyl, X2 = H) (prepn. given) was treated with aq. NaOH in 2-propanol at 80.degree. for 3 h to give 94% I (R1 = R2 = R4 = Me, R3 = SMe, R5 = cyclopentyl, X1 = H), which was oxidized and condensed with 4-pyridinepropanol to give I [R1 = R2 = R4 = Me, R3 = 3-(4-pyridyl)propyloxy, R5 = cyclopentyl, X1 = H].

L5 ANSWER 4 OF 17 REGISTRY COPYRIGHT 2002 ACS
RN 304905-20-2 REGISTRY
CN 1H-Purine, 2-chloro-6,8-dimethyl- (9CI) (CA INDEX NAME)
FS 3D CONCORD
MF C7 H7 Cl N4
SR CA
LC STN Files: CA, CAPLUS



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

2 REFERENCES IN FILE CA (1967 TO DATE)
2 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 135:5583 Reactions of 2-chloro-4,5-diamino-6-methylpyrimidine with 1,3-diketones: formation of new substituted purines. Srinivas, K.; Rao, P. Shanthan; Narsaiah, B.; Rao, J. Madhusudana (Organic Chemistry Division, Indian Institute of Chemical Technology, Hyderabad, 500 007, India). Indian Journal of Chemistry, Section B: Organic Chemistry Including Medicinal Chemistry, 40B(3), 191-194 (English) 2001. CODEN: IJSBDB. ISSN: 0376-4699. Publisher: National Institute of Science Communication, CSIR.

AB Condensation of 2-chloro-4,5-diamino-6-methylpyrimidine (I) with 1,3-diketones gives Schiff bases. These, on cyclization, yield purines. The reaction of I with BzH is also studied.

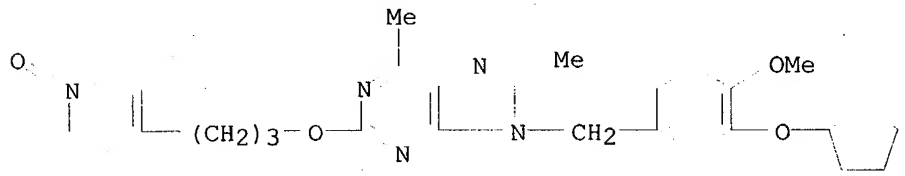
REFERENCE 2: 133:350245 Preparation of purine derivative dihydrate as phosphodiesterase IV inhibitor. Sekiya, Kouichi; Takemiya, Akihiro;

Searched by: Mary Hale 308-4258 CM-1 12D16

Ohshima, Masahiro (Mitsubishi Chemical Corporation, Japan). PCT Int. Appl. WO 2000068231 A1 20001116, 29 pp. DESIGNATED STATES: W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG. (Japanese). CODEN: PIXXD2. APPLICATION: WO 2000-JP2952 20000509. PRIORITY: JP 1999-129499 19990511.

AB Claimed is a dihydrate of 4-[[9-[(3-cyclopentyloxy-4-methoxy)benzyl]-6,8-dimethylpurin]-2-yl-3-oxypropyl]pyridine N-oxide (I); also claimed are : (a) pharmaceutical contg. I as active ingredient; (b) pharmaceutical contg. I as active ingredient for the treatment of asthma, chronic obstructive lung disease and/or other inflammatory diseases; (c) phosphodiesterase IV inhibitor contg. I (d) and intermediates for I. I in vitro showed IC50 of 3.4 x 10-9 M against phosphodiesterase IV, vs. IC50 of 5 x 10-7 M shown by rolipram.

L5 ANSWER 5 OF 17 REGISTRY COPYRIGHT 2002 ACS
RN 304905-19-9 REGISTRY
CN 9H-Purine, 9-[[3-(cyclopentyloxy)-4-methoxyphenyl]methyl]-6,8-dimethyl-2-[3-(1-oxido-4-pyridinyl)propoxy]-, dihydrate (9CI) (CA INDEX NAME)
MF C28 H33 N5 O4 . 2 H2 O
SR CA
LC STN Files: CA, CAPLUS
CRN (225100-00-5)



● 2 H_2O

1 REFERENCES IN FILE CA (1967 TO DATE)
1 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 133:350245 Preparation of purine derivative dihydrate as phosphodiesterase IV inhibitor. Sekiya, Kouichi; Takemiya, Akihiro; Ohshima, Masahiro (Mitsubishi Chemical Corporation, Japan). PCT Int. Appl. WO 2000068231 A1 20001116, 29 pp. DESIGNATED STATES: W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG. (Japanese). CODEN: PIXXD2. APPLICATION: WO 2000-JP2952 20000509. PRIORITY: JP 1999-129499 19990511.

AB Claimed is a dihydrate of 4-[[9-[(3-cyclopentyloxy-4-methoxy)benzyl]-6,8-dimethylpurin]-2-yl-3-oxypropyl]pyridine N-oxide (I); also claimed are : (a) pharmaceutical contg. I as active ingredient; (b) pharmaceutical

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contg. I as active ingredient for the treatment of asthma, chronic obstructive lung disease and/or other inflammatory diseases; (c) phosphodiesterase IV inhibitor contg. I (d) and intermediates for I. I in vitro showed IC50 of 3.4 x 10-9 M against phosphodiesterase IV, vs. IC50 of 5 x 10-7 M shown by rolipram.

L5 ANSWER 6 OF 17 REGISTRY COPYRIGHT 2002 ACS
RN 225100-12-9 REGISTRY
CN 9H-Purine, 2-chloro-9-[[3-(cyclopentyloxy)-4-methoxyphenyl]methyl]-6,8-dimethyl- (9CI) (CA INDEX NAME)
OTHER NAMES:
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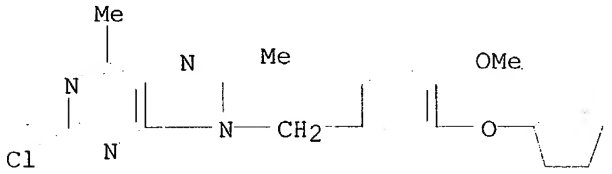

PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

4 REFERENCES IN FILE CA (1967 TO DATE)
4 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 134:252357 Pyrimidine derivatives and method for their preparation. Iwamura, Hiroshi; Tozawa, Takashi; Inokawa, Haruki; Shirasaka, Tadàshi (Mitsubishi Chemical Corp., Japan; Mistubishi Tokyo Pharmaceuticals Inc.). Jpn. Kokai Tokkyo Koho JP 2001089458 A2 20010403, 18 pp. (Japanese). CODEN: JKXXAF. APPLICATION: JP 1999-263372 19990917.
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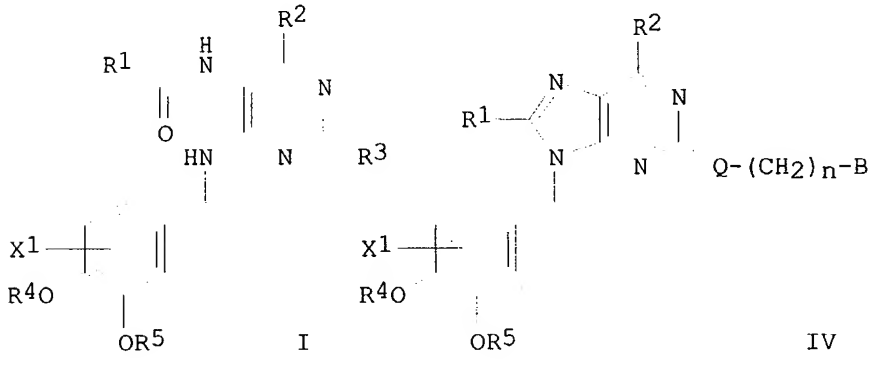

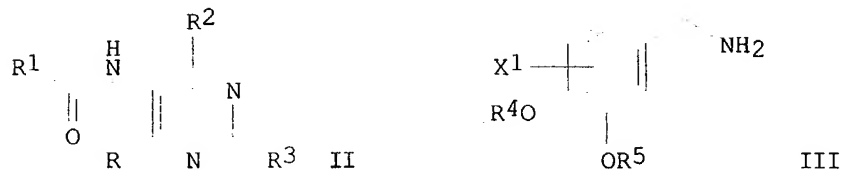

Searched by: Mary Hale 308-4258 CM-1 12D16

AB 5-Acylamino-4-(3,4-dihydroxybenzylamino)pyrimidine derivs. [I; R1, R2 = H, C1-4 alkyl; R3 = (un)substituted C1-10 alkoxy, C6-10 aryloxy, C3-10 cycloalkyloxy, C7-12 aralkyloxy, C1-10 alkylthio, C6-10 arylthio, C3-10 cycloalkylthio, or C7-12 aralkylthio; R4 = C1-4 alkyl, difluoromethyl; R5 = tetrahydropyranyl, C1-7 alkyl, C1-7 haloalkyl, C2-7 alkenyl, bicyclo[2.2.1]hept-2-yl, C3-8 cycloalkyl; X1 = H,halo, NO2] are prepd. by conversion of 4-hydroxy-5-acylaminopyrimidine derivs. (II; R = OH; R1- R3 = same as above) into reactive pyrimidine derivs. II (R = halo, (un)substituted C1-10 alkylsulfonyloxy, C6-10 arylsulfonyloxy, C1-10 dialkyloxyphosphoryloxy, 2,2,2-trifluoroethyloxy; R1-R3 = same as above) and reaction of the latter deriv. with 3,4-dihydroxybenzylamine derivs. (III; R4, R5, X1 = same as above). The above compds. I are useful as intermediates for agrochems. and drugs, in particular 9-(3,4-dihydroxybenzyl)purine antiasthmatics represented by formula [IV; R1, R2, R4 , R5, X1 = same as above; Q = O, S, NHCO, CONH, NH, C1-6 alkyl-NH; n = 0-4; B = (un)substituted Ph, naphthyl, or heterocyclyl; when Q is C1-6 alkyl-NH, n is 1-4 and B is (un)substituted heterocyclyl]. Thus, 4.5 mL Et3N, 12.1 mL POCl3, and 6.50 g 5-acetamido-4-hydroxy-6-methyl-2-methylthiopyrimidine were added to a suspension of 9.62 g benzyltriethylammonium chloride in 65 mL MeCN under ice-cooling and stirred at room temp. for 3 h to give, after workup and silica gel chromatog., 36% 5-acetamido-4-chloro-6-methyl-2-methylthiopyrimidine (V) (2.51 g). Et3N (0.47 mL) was added to a suspension of 350 mg V and 366 mg 3-cyclopentyloxy-4-methoxybenzylamine hydrochloride in 3 mL 2-propanol, heated at 80.degree. with stirring for 3 h, treated with 101 mg 1,4-diazabicyclo[2.2.2]octane, and stirred at 80.degree. for 1.5 to give, after workup and silica gel chromatog., 95% 5-acetamido-4-[(3-cyclopentyloxy-4-methoxybenzyl)amino]-6-methyl-2-methylthiopyrimidine (597 mg). A soln. of the latter compd. (6.04 g) in 50 mL 2-propanol were added 9.3 mL 25% NaOH and 20 mL H2O and stirred at 80.degree. for 3 h to give, after workup, 94% 9-(3-cyclopentyloxy-4-methoxybenzyl)-6,8-dimethyl-2-methylthiopurine.

REFERENCE 2: 134:252207 Preparation of purine derivatives as intermediate for antiasthmatic agents. Iwamura, Hiroshi; Tozawa, Takashi; Inokawa, Haruki; Shirasaka, Tadashi (Mitsubishi Chemical Corp., Japan; Mistubishi Tokyo Pharmaceuticals Inc.). Jpn. Kokai Tokkyo Koho JP 2001089480 A2 20010403, 13 pp. (Japanese). CODEN: JKXXAF. APPLICATION: JP 1999-263373 19990917.

GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB Purines I [R1, R2 = H, C1-4 alkyl; R3 = OH, alkylsulfonyloxy, arylsulfonyloxy, dialkyloxyphosphoryloxy, CF3CH2O, etc.; R4 = C1-4 alkyl, CHF2; R5 = tetrahydrofuranyl, C1-7 (halo)alkyl, C2-7 alkenyl, etc.; X1 = H, halo, NO2], their salts, hydrates, or solvates are prepd. by cyclization of pyrimidines II [R6, R7, R9, R10, X2 = same as R1, R2, R4, R5, X1 in I; R8 = (un)substituted C1-10 alkyloxy, C6-10 aryloxy, C1-10 alkylthio, C6-10 arylthio, etc.], their salts, hydrates, or solvates. II (R6 = R7 = R9 = Me, R8 = SMe, R10 = cyclopentyl, X2 = H) (prepn. given) was treated with aq. NaOH in 2-propanol at 80.degree. for 3 h to give 94% I (R1 = R2 = R4 = Me, R3 = SMe, R5 = cyclopentyl, X1 = H), which was oxidized and condensed with 4-pyridinepropanol to give I [R1 = R2 = R4 = Me, R3 = 3-(4-pyridyl)propyloxy, R5 = cyclopentyl, X1 = H].

REFERENCE 3: 133:350245 Preparation of purine derivative dihydrate as

phosphodiesterase IV inhibitor. Sekiya, Kouichi; Takemiya, Akihiro; Ohshima, Masahiro (Mitsubishi Chemical Corporation, Japan). PCT Int. Appl. WO 2000068231 A1 20001116, 29 pp. DESIGNATED STATES: W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG. (Japanese). CODEN: PIXXD2. APPLICATION: WO 2000-JP2952 20000509. PRIORITY: JP 1999-129499 19990511.

AB Claimed is a dihydrate of 4-[[9-[(3-cyclopentyloxy-4-methoxy)benzyl]-6,8-dimethylpurin]-2-yl-3-oxypropyl]pyridine N-oxide (I); also claimed are : (a) pharmaceutical contg. I as active ingredient; (b) pharmaceutical contg. I as active ingredient for the treatment of asthma, chronic obstructive lung disease and/or other inflammatory diseases; (c) phosphodiesterase IV inhibitor contg. I (d) and intermediates for I. I in vitro showed IC50 of 3.4 x 10-9 M against phosphodiesterase IV, vs. IC50 of 5 x 10-7 M shown by rolipram.

REFERENCE 4: 130:352279 Preparation of purine derivatives as antiasthmatics. Tanaka, Toshihiko; Iwashita, Eiichirou; Tarao, Akiko; Amenomori, Akira; Ono, Yuya (Mitsubishi Chemical Corporation, Japan). PCT Int. Appl. WO 9924432 A1 19990520, 148 pp. DESIGNATED STATES: W: CA, CN, GB, KR, US; RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE. (Japanese). CODEN: PIXXD2. APPLICATION: WO 1998-JP5092 19981112. PRIORITY: JP 1997-310365 19971112.

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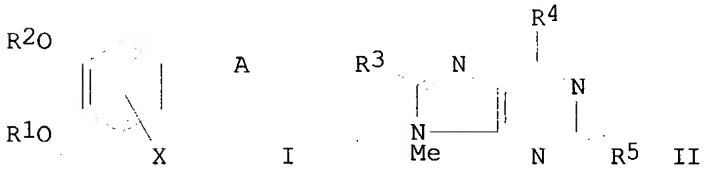

AB Title compds. I and II (R1 = alkyl, CHF2; R2 = tetrahydrofuranyl, alkyl, haloalkyl, alkenyl, cycloalkyl, etc.; R3 = H, halo, OH, alkyl, alkoxy, amino, alkylamino, dialkylamino, etc; R4, R5 = H, halo, alkyl, alkoxy, amino, alkylamino, pyrrolidinyl, morpholino, dialkylamino, etc; X = H, halo, NO2) and their salts, useful as antiasthmatics, were prepd. 2-Chloro-9-[(3-cyclopentyloxy-4-methoxy)benzyl]-6,8-dimethylpurine showed IC50 of 6.7 x 10-9 M against phosphodiesterase IV. Formulations contg. title compds. were given.

L5 ANSWER 7 OF 17 REGISTRY COPYRIGHT 2002 ACS
RN 225100-01-6 REGISTRY
CN 9H-Purine, 9-[[3-(cyclopentyloxy)-4-methoxyphenyl]methyl]-6,8-dimethyl-2-(3-pyridinylmethoxy)- (9CI) (CA INDEX NAME)
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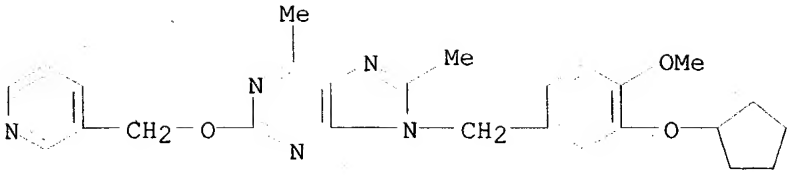
LC STN Files: CA, CAPLUS

Searched by: Mary Hale 308-4258 CM-1 12D16



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1 REFERENCES IN FILE CA (1967 TO DATE)
1 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 130:352279 Preparation of purine derivatives as antiasthmatics. Tanaka, Toshihiko; Iwashita, Eiichirou; Tarao, Akiko; Amenomori, Akira; Ono, Yuya (Mitsubishi Chemical Corporation, Japan). PCT Int. Appl. WO 9924432 A1 19990520, 148 pp. DESIGNATED STATES: W: CA, CN, GB, KR, US; RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE. (Japanese). CODEN: PIXXD2. APPLICATION: WO 1998-JP5092 19981112. PRIORITY: JP 1997-310365 19971112.

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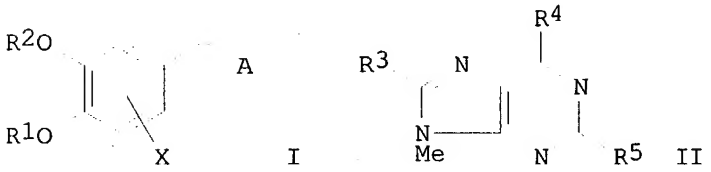

AB Title compds. I and II (R1 = alkyl, CHF2; R2 = tetrahydrofuranyl, alkyl, haloalkyl, alkenyl, cycloalkyl, etc.; R3 = H, halo, OH, alkyl, alkoxy, amino, alkylamino, dialkylamino, etc; R4, R5 = H, halo, alkyl, alkoxy, amino, alkylamino, pyrrolidinyl, morpholino, dialkylamino, etc; X = H, halo, NO2) and their salts, useful as antiasthmatics, were prepd. 2-Chloro-9-[(3-cyclopentyloxy-4-methoxy)benzyl]-6,8-dimethylpurine showed IC50 of 6.7 x 10-9 M against phosphodiesterase IV. Formulations contg. title compds. were given.

L5 ANSWER 8 OF 17 REGISTRY COPYRIGHT 2002 ACS
RN 225100-00-5 REGISTRY
CN 9H-Purine, 9-[[3-(cyclopentyloxy)-4-methoxyphenyl]methyl]-6,8-dimethyl-2-[3-(1-oxido-4-pyridinyl)propoxy]- (9CI) (CA INDEX NAME)
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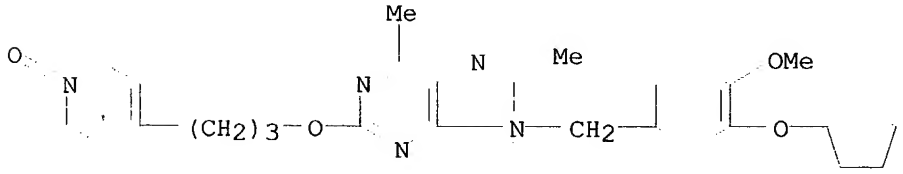
LC STN Files: CA, CAPLUS



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PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

2 REFERENCES IN FILE CA (1967 TO DATE)
2 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 133:350245 Preparation of purine derivative dihydrate as phosphodiesterase IV inhibitor. Sekiya, Kouichi; Takemiya, Akihiro; Ohshima, Masahiro (Mitsubishi Chemical Corporation, Japan). PCT Int. Appl. WO 2000068231 A1 20001116, 29 pp. DESIGNATED STATES: W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG. (Japanese). CODEN: PIXXD2. APPLICATION: WO 2000-JP2952 20000509. PRIORITY: JP 1999-129499 19990511.

AB Claimed is a dihydrate of 4-[[9-[(3-cyclopentyloxy-4-methoxy)benzyl]-6,8-dimethylpurin]-2-yl-3-oxypropyl]pyridine N-oxide (I); also claimed are : (a) pharmaceutical contg. I as active ingredient; (b) pharmaceutical contg. I as active ingredient for the treatment of asthma, chronic obstructive lung disease and/or other inflammatory diseases; (c) phosphodiesterase IV inhibitor contg. I (d) and intermediates for I. I in vitro showed IC50 of 3.4 x 10-9 M against phosphodiesterase IV, vs. IC50 of 5 x 10-7 M shown by rolipram.

REFERENCE 2: 130:352279 Preparation of purine derivatives as antiasthmatics. Tanaka, Toshihiko; Iwashita, Eiichirou; Tarao, Akiko; Amenomori, Akira; Ono, Yuya (Mitsubishi Chemical Corporation, Japan). PCT Int. Appl. WO 9924432 A1 19990520, 148 pp. DESIGNATED STATES: W: CA, CN, GB, KR, US; RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE. (Japanese). CODEN: PIXXD2. APPLICATION: WO 1998-JP5092 19981112. PRIORITY: JP 1997-310365 19971112.

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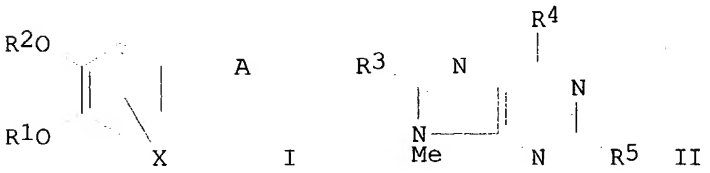

AB Title compds. I and II (R1 = alkyl, CHF2; R2 = tetrahydrofuranyl, alkyl, haloalkyl, alkenyl, cycloalkyl, etc.; R3 = H, halo, OH, alkyl, alkoxy, amino, alkylamino, dialkylamino, etc; R4, R5 = H, halo, alkyl, alkoxy, amino, alkylamino, pyrrolidinyl, morpholino, dialkylamino, etc; X = H, halo, NO2) and their salts, useful as antiasthmatics, were prepd. 2-Chloro-9-[(3-cyclopentyloxy-4-methoxy)benzyl]-6,8-dimethylpurine showed IC50 of 6.7 x 10-9 M against phosphodiesterase IV. Formulations contg. title compds. were given.

L5 ANSWER 9 OF 17 REGISTRY COPYRIGHT 2002 ACS
RN 225099-99-0 REGISTRY
CN 9H-Purine, 9-[[3-(cyclopentyloxy)-4-methoxyphenyl]methyl]-6,8-dimethyl-2-[(3-pyridinylmethyl)thio]- (9CI) (CA INDEX NAME)
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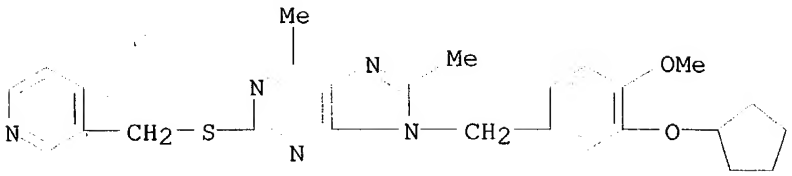
MF C26 H29 N5 O2 S

Searched by: Mary Hale 308-4258 CM-1 12D16

SR CA
LC STN Files: CA, CAPLUS



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1 REFERENCES IN FILE CA (1967 TO DATE)
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REFERENCE 1: 130:352279 Preparation of purine derivatives as antiasthmatics. Tanaka, Toshihiko; Iwashita, Eiichirou; Tarao, Akiko; Amenomori, Akira; Ono, Yuya (Mitsubishi Chemical Corporation, Japan). PCT Int. Appl. WO 9924432 A1 19990520, 148 pp. DESIGNATED STATES: W: CA, CN, GB, KR, US; RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE. (Japanese). CODEN: PIXXD2. APPLICATION: WO 1998-JP5092 19981112. PRIORITY: JP 1997-310365 19971112.

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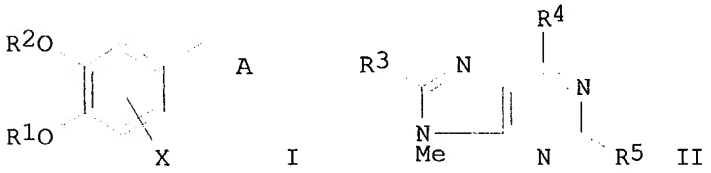

AB Title compds. I and II (R1 = alkyl, CHF2; R2 = tetrahydrofuranyl, alkyl, haloalkyl, alkenyl, cycloalkyl, etc.; R3 = H, halo, OH, alkyl, alkoxy, amino, alkylamino, dialkylamino, etc; R4, R5 = H, halo, alkyl, alkoxy, amino, alkylamino, pyrrolidinyl, morpholino, dialkylamino, etc; X = H, halo, NO2) and their salts, useful as antiasthmatics, were prepd. 2-Chloro-9-[(3-cyclopentyloxy-4-methoxy)benzyl]-6,8-dimethylpurine showed IC50 of 6.7 x 10-9 M against phosphodiesterase IV. Formulations contg. title compds. were given.

L5 ANSWER 10 OF 17 REGISTRY COPYRIGHT 2002 ACS
RN 225099-86-5 REGISTRY
CN 9H-Purine, 9-[[3-(cyclopentyloxy)-4-methoxyphenyl]methyl]-6,8-dimethyl-2-[(1-oxido-3-pyridinyl)methoxy]- (9CI) (CA INDEX NAME)
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MF C26 H29 N5 O4
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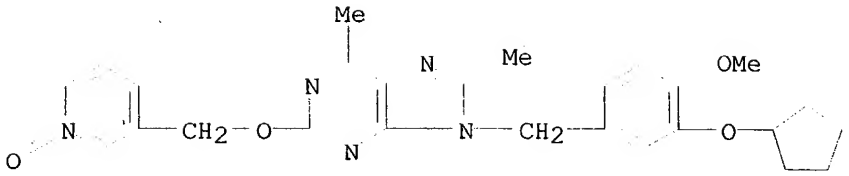
LC STN Files: CA, CAPLUS

Searched by: Mary Hale 308-4258 CM-1 12D16



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

1 REFERENCES IN FILE CA (1967 TO DATE)
1 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 130:352279 Preparation of purine derivatives as antiasthmatics. Tanaka, Toshihiko; Iwashita, Eiichirou; Tarao, Akiko; Amenomori, Akira; Ono, Yuya (Mitsubishi Chemical Corporation, Japan). PCT Int. Appl. WO 9924432 A1 19990520, 148 pp. DESIGNATED STATES: W: CA, CN, GB, KR, US; RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE. (Japanese). CODEN: PIXXD2. APPLICATION: WO 1998-JP5092 19981112. PRIORITY: JP 1997-310365 19971112.

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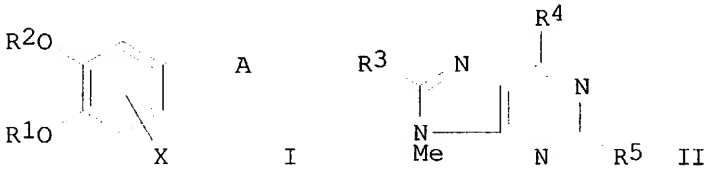
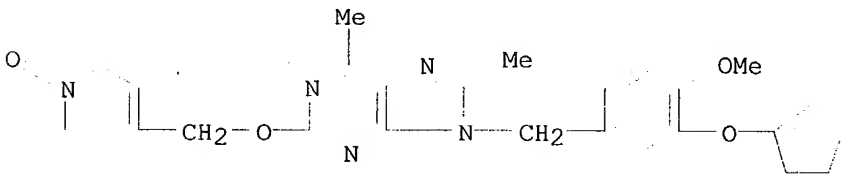


AB Title compds. I and II (R1 = alkyl, CHF2; R2 = tetrahydrofuranyl, alkyl, haloalkyl, alkenyl, cycloalkyl, etc.; R3 = H, halo, OH, alkyl, alkoxy, amino, alkylamino, dialkylamino, etc; R4, R5 = H, halo, alkyl, alkoxy, amino, alkylamino, pyrrolidinyl, morpholino, dialkylamino, etc; X = H, halo, NO2) and their salts, useful as antiasthmatics, were prepd. 2-Chloro-9-[(3-cyclopentyloxy-4-methoxy)benzyl]-6,8-dimethylpurine showed IC50 of 6.7 x 10-9 M against phosphodiesterase IV. Formulations contg. title compds. were given.

L5 ANSWER 11 OF 17 REGISTRY COPYRIGHT 2002 ACS
RN 225099-83-2 REGISTRY
CN 9H-Purine, 9-[[3-(cyclopentyloxy)-4-methoxyphenyl]methyl]-6,8-dimethyl-2-[(1-oxido-4-pyridinyl)methoxy]- (9CI) (CA INDEX NAME)
FS 3D CONCORD
MF C26 H29 N5 O4
SR CA
LC STN Files: CA, CAPLUS



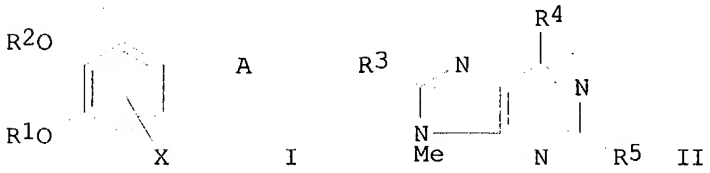
Searched by: Mary Hale 308-4258 CM-1 12D16

PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

1 REFERENCES IN FILE CA (1967 TO DATE)
1 REFERENCES IN FILE CAPLUS (1967 TO DATE)

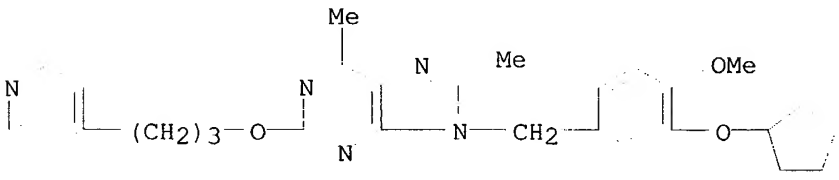
REFERENCE 1: 130:352279 Preparation of purine derivatives as antiasthmatics. Tanaka, Toshihiko; Iwashita, Eiichirou; Tarao, Akiko; Amenomori, Akira; Ono, Yuya (Mitsubishi Chemical Corporation, Japan). PCT Int. Appl. WO 9924432 A1 19990520, 148 pp. DESIGNATED STATES: W: CA, CN, GB, KR, US; RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE. (Japanese). CODEN: PIXXD2. APPLICATION: WO 1998-JP5092 19981112. PRIORITY: JP 1997-310365 19971112.

GI



AB Title compds. I and II (R1 = alkyl, CHF2; R2 = tetrahydrofuranyl, alkyl, haloalkyl, alkenyl, cycloalkyl, etc.; R3 = H, halo, OH, alkyl, alkoxy, amino, alkylamino, dialkylamino, etc; R4, R5 = H, halo, alkyl, alkoxy, amino, alkylamino, pyrrolidinyl, morpholino, dialkylamino, etc; X = H, halo, NO2) and their salts, useful as antiasthmatics, were prepd. 2-Chloro-9-[(3-cyclopentyloxy-4-methoxy)benzyl]-6,8-dimethylpurine showed IC50 of 6.7 x 10-9 M against phosphodiesterase IV. Formulations contg. title compds. were given.

L5 ANSWER 12 OF 17 REGISTRY COPYRIGHT 2002 ACS
RN 225099-81-0 REGISTRY
CN 9H-Purine, 9-[[3-(cyclopentyloxy)-4-methoxyphenyl]methyl]-6,8-dimethyl-2-[3-(4-pyridinyl)propoxy]- (9CI) (CA INDEX NAME)
FS 3D CONCORD
MF C28 H33 N5 O3
SR CA
LC STN Files: CA, CAPLUS, CASREACT



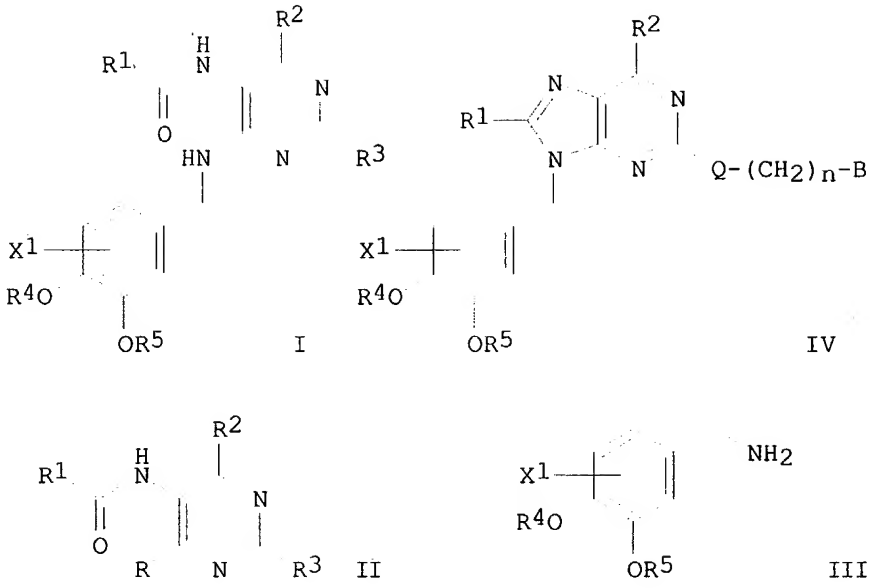
PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

4 REFERENCES IN FILE CA (1967 TO DATE)
4 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 134:252357 Pyrimidine derivatives and method for their preparation. Iwamura, Hiroshi; Tozawa, Takashi; Inokawa, Haruki; Shirasaka, Tadashi (Mitsubishi Chemical Corp., Japan; Mistubishi Tokyo Pharmaceuticals Inc.). Jpn. Kokai Tokkyo Koho JP 2001089458 A2 20010403, 18 pp. (Japanese). CODEN: JKXXAF. APPLICATION: JP 1999-263372 19990917.

Searched by: Mary Hale 308-4258 CM-1 12D16

GI



AB 5-Acylamino-4-(3,4-dihydroxybenzylamino)pyrimidine derivs. [I; R1, R2 = H, C1-4 alkyl; R3 = (un)substituted C1-10 alkoxy, C6-10 aryloxy, C3-10 cycloalkyloxy, C7-12 aralkyloxy, C1-10 alkylthio, C6-10 arylthio, C3-10 cycloalkylthio, or C7-12 aralkylthio; R4 = C1-4 alkyl, difluoromethyl; R5 = tetrahydropyranyl, C1-7 alkyl, C1-7 haloalkyl, C2-7 alkenyl, bicyclo[2.2.1]hept-2-yl, C3-8 cycloalkyl; X1 = H,halo, NO2] are prepd. by conversion of 4-hydroxy-5-acylaminopyrimidine derivs. (II; R = OH; R1- R3 = same as above) into reactive pyrimidine derivs. II (R = halo, (un)substituted C1-10 alkylsulfonyloxy, C6-10 arylsulfonyloxy, C1-10 dialkyloxyphosphoryloxy, 2,2,2-trifluoroethyloxy; R1-R3 = same as above) and reaction of the latter deriv. with 3,4-dihydroxybenzylamine derivs. (III; R4, R5, X1 = same as above). The above compds. I are useful as intermediates for agrochems. and drugs, in particular 9-(3,4-dihydroxybenzyl)purine antiasthmatics represented by formula [IV; R1, R2, R4 , R5, X1 = same as above; Q = O, S, NHCO, CONH, NH, C1-6 alkyl-NH; n = 0-4; B = (un)substituted Ph, naphthyl, or heterocyclyl; when Q is C1-6 alkyl-NH, n is 1-4 and B is (un)substituted heterocyclyl]. Thus, 4.5 mL Et3N, 12.1 mL POCl3, and 6.50 g 5-acetamido-4-hydroxy-6-methyl-2-methylthiopyrimidine were added to a suspension of 9.62 g benzyltriethylammonium chloride in 65 mL MeCN under ice-cooling and stirred at room temp. for 3 h to give, after workup and silica gel chromatog., 36% 5-acetamido-4-chloro-6-methyl-2-methylthiopyrimidine (V) (2.51 g). Et3N (0.47 mL) was added to a suspension of 350 mg V and 366 mg 3-cyclopentyloxy-4-methoxybenzylamine hydrochloride in 3 mL 2-propanol, heated at 80.degree. with stirring for 3 h, treated with 101 mg 1,4-diazabicyclo[2.2.2]octane, and stirred at 80.degree. for 1.5 to give, after workup and silica gel chromatog., 95% 5-acetamido-4-[(3-cyclopentyloxy-4-methoxybenzyl)amino]-6-methyl-2-methylthiopyrimidine (597 mg). A soln. of the latter compd. (6.04 g) in 50 mL 2-propanol were added 9.3 mL 25% NaOH and 20 mL H2O and stirred at 80.degree. for 3 h to give, after workup, 94% 9-(3-cyclopentyloxy-4-methoxybenzyl)-6,8-dimethyl-2-methylthiopurine.

REFERENCE 2: 134:252207 Preparation of purine derivatives as intermediate for antiasthmatic agents. Iwamura, Hiroshi; Tozawa, Takashi; Inokawa,

Haruki; Shirasaka, Tadashi (Mitsubishi Chemical Corp., Japan; Mistubishi Tokyo Pharmaceuticals Inc.). Jpn. Kokai Tokkyo Koho JP 2001089480 A2 20010403, 13 pp. (Japanese). CODEN: JKXXAF. APPLICATION: JP 1999-263373 19990917.

GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB Purines I [R1, R2 = H, C1-4 alkyl; R3 = OH, alkylsulfonyloxy, arylsulfonyloxy, dialkyloxyphosphoryloxy, CF3CH2O, etc.; R4 = C1-4 alkyl, CHF2; R5 = tetrahydrofuranyl, C1-7 (halo)alkyl, C2-7 alkenyl, etc.; X1 = H, halo, NO2], their salts, hydrates, or solvates are prepd. by cyclization of pyrimidines II [R6, R7, R9, R10, X2 = same as R1, R2, R4, R5, X1 in I; R8 = (un)substituted C1-10 alkyloxy, C6-10 aryloxy, C1-10 alkylthio, C6-10 arylthio, etc.], their salts, hydrates, or solvates. II (R6 = R7 = R9 = Me, R8 = SMe, R10 = cyclopentyl, X2 = H) (prepn. given) was treated with aq. NaOH in 2-propanol at 80.degree. for 3 h to give 94% I (R1 = R2 = R4 = Me, R3 = SMe, R5 = cyclopentyl, X1 = H), which was oxidized and condensed with 4-pyridinepropanol to give I [R1 = R2 = R4 = Me, R3 = 3-(4-pyridyl)propyloxy, R5 = cyclopentyl, X1 = H].

REFERENCE 3: 133:350245 Preparation of purine derivative dihydrate as phosphodiesterase IV inhibitor. Sekiya, Kouichi; Takemiya, Akihiro; Ohshima, Masahiro (Mitsubishi Chemical Corporation, Japan). PCT Int. Appl. WO 2000068231 A1 20001116, 29 pp. DESIGNATED STATES: W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG. (Japanese). CODEN: PIXXD2. APPLICATION: WO 2000-JP2952 20000509. PRIORITY: JP 1999-129499 19990511.

AB Claimed is a dihydrate of 4-[[9-[(3-cyclopentyloxy-4-methoxy)benzyl]-6,8-dimethylpurin]-2-yl-3-oxypropyl]pyridine N-oxide (I); also claimed are : (a) pharmaceutical contg. I as active ingredient; (b) pharmaceutical contg. I as active ingredient for the treatment of asthma, chronic obstructive lung disease and/or other inflammatory diseases; (c) phosphodiesterase IV inhibitor contg. I (d) and intermediates for I. I in vitro showed IC50 of 3.4 x 10-9 M against phosphodiesterase IV, vs. IC50 of 5 x 10-7 M shown by rolipram.

REFERENCE 4: 130:352279 Preparation of purine derivatives as antiasthmatics. Tanaka, Toshihiko; Iwashita, Eiichirou; Tarao, Akiko; Amenomori, Akira; Ono, Yuya (Mitsubishi Chemical Corporation, Japan). PCT Int. Appl. WO 9924432 A1 19990520, 148 pp. DESIGNATED STATES: W: CA, CN, GB, KR, US; RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE. (Japanese). CODEN: PIXXD2. APPLICATION: WO 1998-JP5092 19981112. PRIORITY: JP 1997-310365 19971112.

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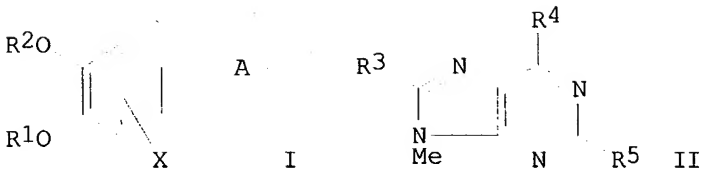

AB Title compds. I and II (R1 = alkyl, CHF2; R2 = tetrahydrofuranyl, alkyl, haloalkyl, alkenyl, cycloalkyl, etc.; R3 = H, halo, OH, alkyl, alkoxy, amino, alkylamino, dialkylamino, etc; R4, R5 = H, halo, alkyl, alkoxy, amino, alkylamino, pyrrolidinyl, morpholino, dialkylamino, etc; X = H, halo, NO2) and their salts, useful as antiasthmatics, were prepd. 2-Chloro-9-[(3-cyclopentyloxy-4-methoxy)benzyl]-6,8-dimethylpurine showed IC50 of 6.7 x 10-9 M against phosphodiesterase IV. Formulations contg. title compds. were given.

L5 ANSWER 13 OF 17 REGISTRY COPYRIGHT 2002 ACS
RN 225099-75-2 REGISTRY
CN 9H-Purine, 9-[[3-(cyclopentyloxy)-4-methoxyphenyl]methyl]-6,8-dimethyl-2-(4-pyridinylmethoxy)- (9CI) (CA INDEX NAME)
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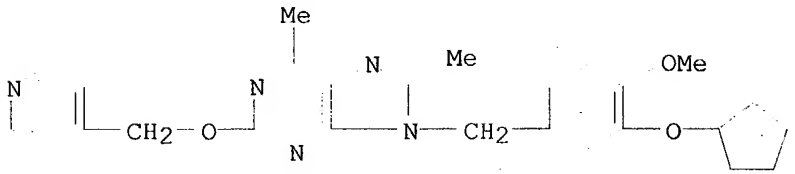
SR CA
LC STN Files: CA, CAPLUS



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

1 REFERENCES IN FILE CA (1967 TO DATE)
1 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 130:352279 Preparation of purine derivatives as antiasthmatics. Tanaka, Toshihiko; Iwashita, Eiichirou; Tarao, Akiko; Amenomori, Akira; Ono, Yuya (Mitsubishi Chemical Corporation, Japan). PCT Int. Appl. WO 9924432 A1 19990520, 148 pp. DESIGNATED STATES: W: CA, CN, GB, KR, US; RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE. (Japanese). CODEN: PIXXD2. APPLICATION: WO 1998-JP5092 19981112. PRIORITY: JP 1997-310365 19971112.

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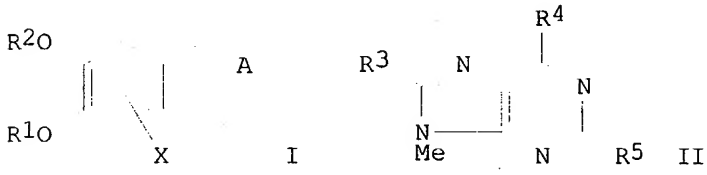

Searched by: Mary Hale 308-4258 CM-1 12D16

AB Title compds. I and II (R1 = alkyl, CHF2; R2 = tetrahydrofuranyl, alkyl, haloalkyl, alkenyl, cycloalkyl, etc.; R3 = H, halo, OH, alkyl, alkoxy, amino, alkylamino, dialkylamino, etc; R4, R5 = H, halo, alkyl, alkoxy, amino, alkylamino, pyrrolidinyl, morpholino, dialkylamino, etc; X = H, halo, NO2) and their salts, useful as antiasthmatics, were prepd. 2-Chloro-9-[(3-cyclopentyloxy-4-methoxy)benzyl]-6,8-dimethylpurine showed IC50 of 6.7 x 10-9 M against phosphodiesterase IV. Formulations contg. title compds. were given.

L5 ANSWER 14 OF 17 REGISTRY COPYRIGHT 2002 ACS
RN 57880-43-0 REGISTRY
CN Acetamide, 2-[(6,8-dimethyl-1H-purin-2-yl)thio]- (9CI) (CA INDEX NAME)
FS 3D CONCORD
MF C9 H11 N5 O S
LC STN Files: BEILSTEIN*, CA, CAPLUS, TOXCENTER
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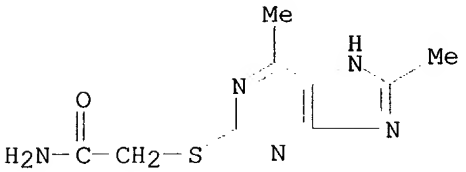

PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

1 REFERENCES IN FILE CA (1967 TO DATE)
1 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 84:17283 Purine studies. XVII. Synthesis of 2-substituted 6,9-di- and 6,8,9-trimethylpurines as amplifiers of phleomycin. Bhushan, Kul; Brown, Desmond J.; Lister, John H.; Stephanson, Lawrence G.; Yoneda, Fumio (John Curtin Sch. Med. Res., Canberra, Aust.). Aust. J. Chem., 28(11), 2553-9 (English) 1975. CODEN: AJCHAS.

GI For diagram(s), see printed CA Issue.

AB 2-(6,8,9-Trimethylpurin-2-ylthio)acetamide (I, R = SCH2CONH2, R1 = Me) and analogous N-substituted acetamides are prepd. by treatment of 6,8,9-trimethylpurine-2-thione with an appropriate 2-chloroacetamide. 6,9-Dimethyl-2-(piperidin-1-yl)purine I(R = piperidino, R1 = H) and some 2-polymethyleneamino homologues are made by initial amination of 2-chloro-4-methyl-6-methylamino-5-nitropyrimidine followed by redn. of the nitro group and final cyclization with HCO2H. Such purines enhance the lethal effect of phleomycin on Escherichia coli cultures.

L5 ANSWER 15 OF 17 REGISTRY COPYRIGHT 2002 ACS
RN 52379-87-0 REGISTRY
CN 1H-Purine, 6-ethyl-8-methyl-2-(methylthio)- (9CI) (CA INDEX NAME)
FS 3D CONCORD
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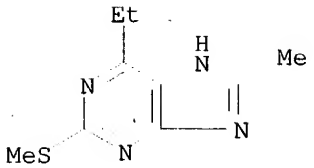
LC STN Files: BEILSTEIN*, CA, CAPLUS
(*File contains numerically searchable property data)

Searched by: Mary Hale 308-4258 CM-1 12D16



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

2 REFERENCES IN FILE CA (1967 TO DATE)
2 REFERENCES IN FILE CAPLUS (1967 TO DATE)

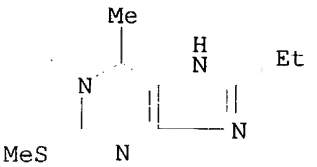
REFERENCE 1: 82:68750 Purines as amplifiers of the antibiotic activity of phleomycin against Escherichia coli B. Angyal, Annette M.; Grigg, G. W.; Badger, R. J.; Brown, D. J.; Lister, J. H. (Div. Anim. Genet., CSIRO, Epping, Aust.). J. Gen. Microbiol., 85, Pt 1, 163-8 (English) 1974. CODEN: JGMIAN.

AB The potentiation activities of purine [120-73-0] and 63 of its derivs. on the antibacterial activity of phleomycin [11006-33-0] were investigated with E. coli, and some tentative correlations between structure and activity were discussed. The inhibitory effect of phleomycin was greatly increased by some of the derivs., presumably as a result of their ability to enhance local denaturation around phleomycin-thymine complexes in the bacterial DNA. The lack of correlation between potentiating activity of the derivs. and their partition coeff. between octanol and water indicated that passage through a fatty barrier was not a critical factor in their activity.

REFERENCE 2: 80:133383 Purine studies. X. Further synthetic approaches to purines for the amplification of phleomycin activity against Escherichia coli. Badger, Rodney J.; Brown, Desmond J.; Lister, John H. (John Curtin Sch. Med. Res., Canberra, Aust.). J. Chem. Soc., Perkin Trans. 1 (1), 152-8 (English) 1974. CODEN: JCPRB4.

AB Analogs of 6,9-dimethyl-2(methylthio)purine, which enhances the activity of phleomycin against E. coli, were prepd. having the C- or N-Me group replaced by an Et group, having an addnl. 8-Me or 8-Et group, or lacking the C- or N-Me group. Related 2-(ethylthio)- and 2-(dimethylamino)purines were also prepd. as were 2-[(carbamoylmethyl)thio]- and 2-(methylsulfonyl)-6,9-dimethylpurine. S-Methylation of 6-ethyl-9-methylpurine-2(3H)-thione gave mainly bis(6-ethyl-9-methylpurin-2-yl) sulfide.

L5 ANSWER 16 OF 17 REGISTRY COPYRIGHT 2002 ACS
RN 50680-77-8 REGISTRY
CN 1H-Purine, 8-ethyl-6-methyl-2-(methylthio)- (9CI) (CA INDEX NAME)
FS 3D CONCORD
MF C9 H12 N4 S
LC STN Files: BEILSTEIN*, CA, CAPLUS
(*File contains numerically searchable property data)



Searched by: Mary Hale 308-4258 CM-1 12D16

PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

3 REFERENCES IN FILE CA (1967 TO DATE)
3 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 82:68750 Purines as amplifiers of the antibiotic activity of phleomycin against Escherichia coli B. Angyal, Annette M.; Grigg, G. W.; Badger, R. J.; Brown, D. J.; Lister, J. H. (Div. Anim. Genet., CSIRO, Epping, Aust.). J. Gen. Microbiol., 85, Pt 1, 163-8 (English) 1974. CODEN: JGMIAN.

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AB Analogs of 6,9-dimethyl-2(methylthio)purine, which enhances the activity of phleomycin against E. coli, were prepd. having the C- or N-Me group replaced by an Et group, having an addnl. 8-Me or 8-Et group, or lacking the C- or N-Me group. Related 2-(ethylthio)- and 2-(dimethylamino)purines were also prepd. as were 2-[(carbamoylmethyl)thio]- and 2-(methylsulfonyl)-6,9-dimethylpurine. S-Methylation of 6-ethyl-9-methylpurine-2(3H)-thione gave mainly bis(6-ethyl-9-methylpurin-2-yl) sulfide.

REFERENCE 3: 79:146486 Purine studies. VIII. Formation of alkylthiopurines from 4,5-diaminopyrimidine- or purinethiones by means of ortho ester-anhydride mixtures. Badger, Rodney J.; Brown, Desmond J.; Lister, John H. (John Curtin Sch. Med. Res., Canberra, Aust.). J. Chem. Soc., Perkin Trans. 1 (17), 1906-9 (English) 1973. CODEN: JCPRB4.

GI For diagram(s), see printed CA Issue.

AB Purinethiones with tri-Et ortho ester-anhydride mixts. gave the corresponding 2-(ethylthio)purines. E.g. 8-methylpurine-2-thione (I, R = Me) with EtC(OEt)3(EtCO)2O gave 78% 2-(ethylthio)-8-methylpurine (II, R = Me). Similarly 4,5-diaminopyrimidine-2-thione with RC(OEt)3-(EtCO)2O (R = Me, Et, and Ph) gave the corresponding mixts. of I and II. 2- and 4-Thiouracil with EtC(OEt)3-(EtCO)2O gave the corresponding S- and N-1-, and S- and N-3-Et derivs. resp.

L5 ANSWER 17 OF 17 REGISTRY COPYRIGHT 2002 ACS
RN 37796-31-9 REGISTRY
CN 1H-Purine, 6,8-dimethyl-2-(methylthio)- (9CI) (CA INDEX NAME)
FS 3D CONCORD
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LC STN Files: BEILSTEIN*, CA, CAPLUS
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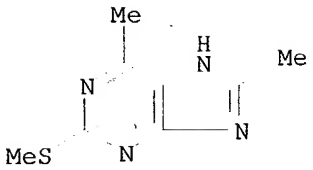
Searched by: Mary Hale 308-4258 CM-1 12D16



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

2 REFERENCES IN FILE CA (1967 TO DATE)
2 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 82:68750 Purines as amplifiers of the antibiotic activity of phleomycin against Escherichia coli B. Angyal, Annette M.; Grigg, G. W.; Badger, R. J.; Brown, D. J.; Lister, J. H. (Div. Anim. Genet., CSIRO, Epping, Aust.). J. Gen. Microbiol., 85, Pt 1, 163-8 (English) 1974. CODEN: JGMIAN.

AB The potentiation activities of purine [120-73-0] and 63 of its derivs. on the antibacterial activity of phleomycin [11006-33-0] were investigated with E. coli, and some tentative correlations between structure and activity were discussed. The inhibitory effect of phleomycin was greatly increased by some of the derivs., presumably as a result of their ability to enhance local denaturation around phleomycin-thymine complexes in the bacterial DNA. The lack of correlation between potentiating activity of the derivs. and their partition coeff. between octanol and water indicated that passage through a fatty barrier was not a critical factor in their activity.

REFERENCE 2: 77:114363 Purine studies. VII. Synthesis of purines as amplifiers of phleomycin against Escherichia coli. Brown, D. J.; Jones, R. L.; Angyal, Annette M.; Grigg, G. W. (Dep. Med. Chem., John Curtin Sch. Med. Res., Canberra, Aust.). J. Chem. Soc., Perkin Trans. 1 (14), 1819-25 (English) 1972. CODEN: JCPRB4.

AB Methyl-, alkylthio-, methoxy-, and dimethylamino-substituted purines [e.g. 2,6,9-trimethyl-, 2-(dimethylamino)-6,8,9-trimethyl-, 2-methoxy-6,9-dimethyl-, and 2-(ethylthio)-6,9-dimethylpurine] were prepd. and tested as amplifiers of phleomycin against E. coli. 6,9-Dimethyl-2-(methyl-14C-thio)purine was prepd.; administered to mice it reached the urine as the corresponding sulfoxide.

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